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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LIETO, LOUIS D	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/381,344	SEEMANN ET AL.	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/26/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-12,16-18 and 23-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-12,16-18 and 23-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/26/05 has been entered.

DETAILED ACTION

Applicant's arguments filed 10/26/05 have been fully considered but they are not persuasive. The amendment has been entered. Claims 9-12, 16-18 and 23-32 are pending. Applicant amended claims 9 and 10, and cancelled claims 5-8 and 13-15. The sections of 35 U.S.C. not included in this office action can be found in a previous office action. An action on the merits follows.

Claims 9-12, 16-18 and 23-32 are currently under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-12,16-18,23-25 and 29-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims have been amended so that they now contain subject matter, which was not described in the specification in such a way

as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The original disclosure fails to recite the limitations of "wherein said immunosuppressant is administered before...administration of the transgenic product into the mammal" (Claim 16). The phrase transgenic product indicates that applicant's claim is presently drawn to administration of the product of the transgene with an immunosuppressant. However, the rest of the claim is drawn to administration of the transgene, and not the product. It would be remedial to amend line 10 of claim 16 to read on "administration of the transgene into the mammal." Further, the original disclosure fails to recite the limitations of "wherein said immunosuppressant is administered before...administration of the transgenic cells" (Claim 29). Claim 29 and its dependents are presently drawn to a method of *ex vivo* therapy. Applicants have not indicated where in the specification support for this new limitation can be found. Based on the disclosure as filed a practitioner in the art would not be able to determine that the inventors contemplated either administration of the transgenic product into the mammal or administration of the transgenic cells at the time of filing. Further, a key word search of the specification fails to find disclosure of these limitations anywhere in the specification as initially filed. Therefore, since the specification as filed doe not contain support for the terms administration of the transgenic product into the mammal or administration of the transgenic cells; they are considered to be new matter. See M.P.E.P. 608.04(a). This new rejection is necessitated by applicant's amendment to the claims. Claims 9-12,17,18, and 23-25 depend from claim 16. Claims 30-32 depend from claim 29. The

Claims 9-12, 16-18 and 23-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 26-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing the tolerance of a mammal to a vector carrying a transgene, wherein a vector, carrying a transgene is administered to a mammal, before, during or after the administration of p15-deoxyspergualin to the mammal intravenously or intraperitoneally, wherein said transgene encodes a protein, wherein administration of p15-deoxyspergualin is discontinued, and the transgene expression levels are 50% greater, at 15 days after discontinuation of the DSG, than in a mammal that did not receive DSG, does not reasonably provide enablement for increasing tolerance in a mammal to transgenic cells produced in vitro or wherein the transgene of the transgenic cells produces a therapeutic protein that effects a treatment of a disease or wherein the transgenic cell produced in vivo after administration of a vector in vivo produce treatment of any disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are presently drawn to three independent claims and their dependents. Claims 9-12, 16-18 and 23-25 encompass a method for expressing any transgenic product in any mammal comprising administering any transgene, by any means to any cell of the mammal, *in vitro* or *in vivo*, wherein the immunosuppressant p15-deoxyspergualin (DSG) is administered before, during or after the administration of the transgenic product into the mammal. Wherein the

DSG may be administered by a variety of routes into a mammal such as a man, and the transgene expression levels are 50%, 5 times or 10 times greater, at 15 days after discontinuation of the DSG, than in a mammal that did not receive DSG. It is again noted that the there is no support in the specification as filed for the administration of the transgenic product into the mammal.

Claims 26-29 encompass a method for increasing tolerance to transgenic product in any mammal comprising administering any transgene, by any means to any cell of the mammal, *in vivo*, wherein the immunesuppressant p15-deoxyspergualin (DSG) is administered before, during or after the administration of the vector. Wherein the DSG may be administered intravenously into a mammal such as a man, and the transgene expression levels are 50% greater, at 15 days after discontinuation of the DSG, than in a mammal that did not receive DSG.

Claims 29-32 encompass a method for increasing tolerance to transgenic cells in any mammal comprising administering any transgene, by any means to any cell of the mammal, wherein the immunesuppressant p15-deoxyspergualin (DSG) is administered before, during or after the administration of the transgenic cells. Wherein the DSG may be administered intravenously into a mammal such as a man, the cells may transfected *in* vivo, and the transgene expression levels are 50% greater, at 15 days after discontinuation of the DSG, than in a mammal that did not receive DSG.

It is noted that the invention claimed in claim 16 and its dependents is not supported by the specification as filed or the art of record. The claim language is somewhat contradictory, however it has been interpreted as the transfection of a mammals cells *ex vivo*, followed by the administration of the resulting transgenic product from these cells to the mammal before, during or after the administration of DSG. However, the specification does not provide any guidance on

how to practice the invention as claimed. There is no guidance in the specification on the ex vivo transfection of any cells, using any vector, the isolation of any transgenic product from said cells, or the administration of any transgenic product to any mammal. Therefore the invention as presently claimed in claim 16 and its dependents is not enabled by the specification.

The specification on pages 2-5 provides a general description of using immunosuppressants for increasing tolerance of transgenic cells in a mammal, and lists different immunosuppressants, different protein that are therapeutic and different diseases. The specification also provides a general approach of treating a disease using gene therapy approach *in vivo* or *in vitro,* or by DNA vaccination. However it is noted that the specification does not provide any specific guidance on any method of using transgenic mammals cells in *ex vivo* gene therapy. The specification also states that the immunosuppressant of the claimed invention could be administered by different routes. However, it is noted that the specification does not provide any guidance as to how a transgenic cells would be prepared in vitro or how a transgenic cell would be administered to a mammal or what doses of the cell would be used or as to how the pharmaceutical p15-deoxyspergualin would be administered to a mammal intranasaly, topically, subcutaneously, topically, by inhalation or by other routes of administration. It is noted that out of the listed routes of administration (claim 9), the art of record only teaches administration of DSG by intravenous infusion (see page 4 in reference # 16 of the IDS filed 5-31-01) or i.p injection. DSG is the dehydroxylated derivative of spergualin, a metabolite of *Bacillus laterosporus*, and is known to be ineffective as an immunosuppressant when given orally {Gruber et al. (1997) Journal of Surgical Research 71:137-144; pg. 137, col. 2}. In other words, neither the prior art nor the specification teaches as how an artisan would have administered

DSG by the routes recited in claim 9, therefore, an artisan of skill would have be carry out extensive experimentation to administer DSG and determine whether DSG would be able to produce its immunosuppressant effect when administered by different routes or what doses would be required to produce the increase in tolerance or expression.

Next the specification describes two examples. Example 1 teaches that in 50% animals (mice) that were treated with DSG only for 5 days after vector administration, 10% of the maximal expression of the transgene was observed on the 42nd day. The specification cites a PNAS paper for the recombinant adenovirus used in the experiment (see lines 35-39 of page 8 of the specification). It is noted that the cited paper teaches construction of adenovirus vectors that have deletions or insertions in the E1 or E3 regions, which indicates that different vectors of the paper would produce different levels of immune response. Example 2 describes the effect of DSG on alpha 1-antitrypsin expression by adenoviral vector in a NMRI mouse. Administration of DSG by i.p. for 5 days resulted in about 6 fold difference in the serum level of alpha 1-antitrypsin at almost all of the different time intervals studied (see columns 4 and 5 in table 1). However, when comparing the results of example 1 and 2, there was about 50% level of the maximum expression level (day 30) in the DSG treated group. These results indicate that there is an effect of the transgene used. It is noted that the specification discloses that alpha 1-antitrypsin used in example 2 is not antigenic. Therefore, one could assume that the higher protein levels in example 2 could be due to lack of antigenicity of the transgene product. In other words, the protection produced by DSG would depend on the protein encoded by the transgene. Tripathi et al. observed that immune response directed against foreign transgene-encoded proteins are the major determinants of the stability of gene expression following

intramuscular injection of recombinant adenoviral vector (see the abstract). The specification does not provide sufficient evidence as to whether the protection produced is due to antigenicity of the protein product or because of the adenoviral antigenicity and therefore an artisan would have to carry out experimentation of trial and error to determine whether DSG would have provided protection when different transgene were used in the claimed method. Adenoviruses are known to induce potent immune responses which can drastically reduce the efficacy of present/further adenoviral treatments. These effects are generally not observed with plasmid vectors. It is unclear from the specification that administration of DSG and the suppression of an immune response will have any effect on transgene expression from non-adenoviral vectors. Regarding adenoviral vector mediated gene therapy, Trapnell et al noted that the factors that affect the host immune response are: the dose of the vector; the route of administration; the level of replication (if replicating vector); the nature of the transgene contained in the recombinant vector; the genetic and physiological characteristics of the host; and the existence and level of pre-existing immune responses to previously administered adenovirus vectors (see page 12, last but one paragraph in Trapnell et al. WO96/12406, 5-2-1996). It is noted that DSG prevents humoral antibody response against adenoviral vector however, it is not known whether DSG also prevents other host immune response, inflammatory responses and even in case of humoral response, in the absence of any teachings from the specification as to what doses of adenovirus would be used, an artisan would not know as to what doses of DSG to use so as to increase transgene expression.

In summary, the state of the art of transgenic cell transplantation in a mammal or in man is unpredictable for several limitations as discussed above and therefore, in view of the breadth

of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, one of ordinary skill in the art at the time of the invention would have required an undue amount of experimentation to make and use the claimed invention commensurate with the scope of the claimed invention. Accordingly, limiting the scope of the claimed invention to a method of increasing the tolerance of a mammal to a vector carrying a transgene, wherein a vector, carrying a transgene is administered to a mammal, before, during or after the administration of p15-deoxyspergualin to the mammal intravenously or intraperitoneally, wherein said transgene encodes a protein, wherein administration of p15-deoxyspergualin is discontinued, and the transgene expression levels are 50% greater, at 15 days after discontinuation of the DSG, than in a mammal that did not receive DSG, is proper.

Response to Arguments

Applicant's arguments filed 10/26/05 have been fully considered but they are not persuasive. The previous office action identified the following issues of record: **1)** lack of enablement for administration of, or increasing the tolerance of, transgenic cells in any mammal including a man wherein the transgenic cells were from the same or different species expressed any gene or where the method was for treating any disease by gene therapy or by ex vivo cell therapy; **2)** lack of enabling disclosure for how a transgenic cells would be prepared in vitro or how a transgenic cell would be administered to a mammal or what doses of the cell would be used; **4)** lack of enabling disclosure as to what doses of the DSG would be used or what routes of administration would be used or which transgene would be used such that the effect of the transgene induced immune response is decreased by DSG treatment; **5)** lack of enablement for the claimed method when transgenic cells are transplanted in a mammal or in a man, except for

autologous cell transplantation which would produce minimal immune response; and **6)** lack of enablement for a method of gene therapy.

1 &5) The rejections of record based on issues **1** and **5** are withdrawn in view of applicant's arguments and amendments to the claims

2) Applicant's arguments and amendements have generally addressed the basis of the rejection over issue **2**. However, upon further consideration it has been determined that the specification as filed does not provide any guidance on using the claimed method in *ex vivo* gene therapy. See above.

4) Applicants cancellation of claims 5-8 and 13-15 have overcome the issues of rejection related to lack of enabling disclosure as to how the methods of treatment of diabetes or AIDS, or DNA vaccination would be carried out. Applicant argues that the specification describes routes of administration and dosages of DSG and other immuosuppresants to enable practitioner to practice the invention in a manner commensurate in scope with the claims. However, it is again noted that applicant only provides guidance on two routes of administration of DSG in the claims. Further, in view of the art of record, the skilled practitioner would be unable to determine how to successfully administer DSG by routes other than intravenous or i.p. Injection. See above. This is due to the fact that DSG is not effective by any route of administration. Therefore without specific guidance in the specification as to the practice of the claimed invention via any of the routes of administration in claim 9, the skilled practitioner would be unable to predict how to practice the invention as claimed without undue and extensive experimentation. Case law teaches (Ex parte Forman, 230 USPQ 546,547 (BPAI 1986)) that "the disclosure of a patent application must enable practice of the invention claimed without undue experimentation", wherein factors

involved in the determination of undue experimentation were deemed to include "the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims." Further, "case law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not to find out how to use it for themselves." In re Gardner 166 USPQ 138 (CCPA) 1970. For these reasons of record and those stated in the previous action the rejection over issue **4** is maintained.

6) Applicant has cancelled claims 5-8 and 13-15 that were drawn to specific methods of gene therapy. The remaining claims are drawn to general methods of improving the level of expression of a transgene and increasing mammalian tolerance to a transgene by administering DSG to the mammal concomitantly with the transgene. Since these claims are not drawn to specific therapeutic methods the rejection over issue **6** is withdrawn.

Rejections based on the second paragraph of 35 U.S.C. 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

The rejection of amended claim 16 under 35 U.S.C 112, second paragraph for being vague and indefinite is withdrawn. Applicant's amendments filed 10/26/2005 have been fully considered and are persuasive.

Claims 9-12,16-18,23-25 and 29-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 recites the limitation "wherein said immunosuppressant is administered before, during, or after, or any combination thereof, administration of the transgenic product into the mammal" in lines 8-10. There is insufficient antecedent basis for this limitation in the claim. The claim is drawn to a method for expressing a transgenic product in a mammal. There is insufficient antecedent basis for administering any transgenic product.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: administration of the transgenic product into the mammal. Claims 10-12,16-18,23-25 depend from claim 16.

Claim 16 recites the limitation "introducing into a cell of said mammal a transgene capable of expressing said transgenic product" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim. It would be remedial to amend the claim to: "introducing into a cell of the mammal a transgene capable of expressing the transgenic product."

Claim 29 recites the limitation "introducing into a cell of said mammal a transgene capable of expressing said transgenic product" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim. It would be remedial to amend the claim to: "introducing into a cell of the mammal a transgene capable of expressing the transgenic product."

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP

§ 2172.01. The omitted steps are: administration of transgenic cells to the mammal. Claims 30-32 depend from claim 29.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

It is noted that the prior rejections of record over Smith et al. and alternatively Trapnell et al. were incorrectly made under 35 USC 102(a). The claims of record are properly rejected over these references under 35 USC 102(b). Please note that the filing date of the foreign priority document is not the effective filing date, although the filing date of the foreign priority document may be used to overcome certain references. See MPEP § 706.02(b) and § 2136.05.

It is also noted that in the advisory action of 9/19/05 the examiner indicated that applicant's amendments to the claims were sufficient to overcome the teachings in the art. However upon further consideration it has been determined that the examiner's statement was made pre-maturely. The rejections are therefore maintained, see below.

Claims 26-28 are rejected under 35 U.S.C. 102(b) as anticipated by Smith et al. (Gene Therapy 3:496-502, 1996).

Smith et al teaches use of transient immunosuppression with DSG in mice injected intravenously with adenoviral vector carrying the beta-galactosidase gene. Smith et al administered DSG intravenously to the mice at time of the exposure of the adenovirus (see the abstract), and observed that administration of DSG permitted 100 fold increase in expression of factor IX vector after administration of a second adenovirus encoding factor IX vector , compared to a mouse that did not receive DSG (pg. 498, Figure 2, pg. 499, Figure 3). Measurements were taken 35 days after the cessation of DSG treatment. Wherein, the adenoviral vectors were E1a, E3-deleted vectors (pg. 500, Materials and Methods). Therefore, by teaching all the limitations of the claims as written, Smith et al. clearly anticipates the instant invention as claimed.

It is noted that applicant's claims contain the limitation that the level of transgenic product, measured 15 days after the discontinuation of said administration of the immunosuppressant, is at least 50% greater than the level when said immunosuppressant is not administered, and may be 5 or 10 times greater. However, the method steps of Smith et al. anticipate the steps of the invention as claimed, and as disclosed in the specification in that DSG is intravenously injected into mice in order to induce immuosuppression to adenovirus mediated gene therapy. It is noted that claims 26-28 state specific levels of expression. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of

proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Thus applicant needs to provide evidence or arguments that the prior art would not lead to these particularly stated expression levels.

Claims 26-28 are rejected under 35 U.S.C. 102(b) as anticipated by Trapnell et al (WO 96/12406, 05-02-1996).

Trapnell et al teaches a method of administering to a host concurrently with an adenoviral vector that expresses a therapeutic gene of interest and immunosuppressive agents, such as DSG (see the entire document). Example 3 discloses administration of DSG i.p. once daily beginning the day before administration and continuing for a total of eight days (see page 33, last paragraph). Figure 17 of Trapnell et al shows the human factor IX levels in mice that were administered adenoviral vector expressing factor IX alone or along with DSG or other immunosuppressants. Page 42 (last paragraph) discloses that five weeks after vector administration, no detectable levels of neutralizing antibodies were observed. Trapnell et al also discloses that DSG immunosuppression also allows re-administration of the adenoviral vector (see the last paragraph on page 44 continued on page 45). Claim 1 of Trapnell et al recites a method of gene therapy treatment by administering to a host an adenoviral vector including at least one DNA sequence encoding a therapeutic protein and an immunosuppressive agent and discontinuing administration of said adenoviral vector and said immunosuppressive agent. Claims 10-11, and 14 recite that the immunosuppressive agent is DSG. Claims 19-21 recite that

the immunosuppressive agent is administered prior to, at the same time or after the administration of the adenoviral vector. It is noted that while the claims of Trapnell et al. recite re-administration of the vector and DSG, DSG administration is only provided for a certain period of time and then discontinued (see page 33, last paragraph). Therefore, by teaching all the limitations of the claims as written, Trapnell et al. clearly anticipates the instant invention as claimed.

It is noted that applicants claims contain the limitation that the level of transgenic product, measured 15 days after the discontinuation of said administration of the immunosuppressant, is at least 50% greater than the level when said immunosuppressant is not administered, and may be 5 or 10 times greater. However, the method steps of Trapnell et al. anticipate the steps of the invention as claimed, and as disclosed in the specification in that DSG is intravenously injected into mice in order to induce immuosuppression to adenovirus mediated gene therapy. It is noted that claims 26-28 state specific levels of expression. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke, supra. Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). Thus

applicant needs to provide evidence or arguments that the prior art would not lead to these particularly stated expression levels.

Examiner's Comment

Claim 16 and its dependents are not present anticipated by the references of record as discussed above, because claim 16 is drawn to the administration of a transgenic product (e.g. a protein) to the mammal. Applicant's amendment of claim 16 to, the administration of a transgene to the mammal, would lead to the rejection of claim 16 and its dependents based on the references cited above.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101, which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

The objection of claim 25 under 37 CFR 1.75 as being a substantial duplicate of claim 28 is withdrawn because of applicant's amendment to the claims.

No claims allowed.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier

communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that can be viewed in the PAIR can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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